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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/341,600	09/15/1999	ALAN BERRY	3161-18-PUS	5327

22442 7590 07/30/2002

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 07/30/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/341,600	Berr et al.
Examiner	**Art Unit**
Christian L. Fronda	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 40-70 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 40-70 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 5/20/2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/341,600 is acceptable and a CPA has been established. An action on the CPA follows.

2. Claims 40-70 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 40-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for making glucosamine by fermentation using a microorganism which has a genetic modification which reduces glucosamine-6-phosphate synthase product inhibition, wherein the nucleic acid encoding glucosamine-6-phosphate synthase product inhibition is mutated using random PCR, does not reasonably provide enablement for any microorganism comprising any genetic modification that increases glucosamine-6-phosphate synthase action; any genetic modification in a nucleic acid sequence encoding glucosamine-6-phosphate synthase that increases glucosamine-6-phosphate synthase action; and any genetic modification selected from the group consisting of deletion, insertion, inversion, substitution, and derivatization of at least one nucleotide which results in increased glucosamine-6-phosphate synthase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants' arguments filed January 19, 2001 (paper no. 14), have been fully considered but they are not persuasive. Applicants argue that the specification is enabling and that it is not necessary to have prior knowledge of the amino acid sequence of the claimed glucosamine-6-phosphate synthase in order to obtain mutants with the desired property of increased enzyme activity.

The nature and breadth of the claims encompass any microorganism comprising any genetic modification that increases glucosamine-6-phosphate synthase action. The specification

provides guidance and examples in substituting one amino acid at position 4, 272, 450, 39, 250, 472, or 469 of SEQ ID NO: 16 which is from *E. coli*. However, the specification does not provide guidance in making any microorganism comprising any genetic modification that increases glucosamine-6-phosphate synthase action; any genetic modification in a nucleic acid sequence encoding glucosamine-6-phosphate synthase; or an amino acid modification to the amino acid sequence of any glucosamine-6-phosphate synthase selected from the group consisting of deletion, insertion, inversion, substitution, and derivatization which results in increased glucosamine-6-phosphate synthase action.

The amount of experimentation to obtain the claimed microorganism for use in the production of glucosamine is undue because one skilled in the art would have to select a type of genetic modification out of a vast number of modifications to perform on the claimed microorganism, such as replacing the wild-type promoter of glucosamine-6-phosphate synthase with a high expression promoter, deleting, inserting, substituting, derivatizing, or combinations thereof to the amino acid sequence of glucosamine-6-phosphate synthase, or selecting proteins and enzymes other than glucosamine-6-phosphate synthase to genetically modify; expressing the glucosamine-6-phosphate synthase mutant, measuring the activity of said mutant; and determining whether the selected mutation results in an increase in glucosamine-6-phosphate synthase action. Applicants have not shown that any mutation in any protein or enzyme other than the mutation of glucosamine-6-phosphate synthase having the amino acid residue at position 4, 272, 450, 39, 250, 472, or 469 of SEQ ID NO: 16 replaced with another amino acid residue would result in a microorganism which has increased glucosamine-6-phosphate activity.

Since routine experimentation in the art does not include making a vast number of glucosamine-6-phosphate synthase mutants, and screening and selecting said mutants that have an increase in glucosamine-6-phosphate synthase action where the expectation of obtaining the desired mutation which results in an increase in glucosamine-6-phosphate synthase action is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as the specific type of genetic modification to perform on the specific proteins or enzymes of claimed microorganism, the amino acid residues which can be modified that lead to the claimed effect, or the gene encoding the said synthase and its biological source. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 40-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 40 (i), the phrase "encoding glucosamine-6-phosphate synthase which has glucosamine-6-phosphate synthase activity" is confusing since the nucleic acid encodes that enzyme and the nucleic acid itself does not have any enzymatic activiy. Claims 41-70 which depend from claim 40 are also rejected because they do not correct the defect of claim 40.

Conclusion

7. No claim is allowed.

8. This is a CPA of applicants' earlier Application No. 09/341,600. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The paper copy of the "Sequence Listing" does not match the "Sequence Listing" in computer readable form. The computer readable form of the "Sequence Listing" states that there are four sequences (SEQ ID NOs: 1-4). However, the paper copy of the "Sequence Listing" only shows one sequence (SEQ ID NO: 1).

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ A substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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